

A drugs company runs hundreds of tests called clinical trials every year to test how efficient and safe their medicines are. But they aren't required to publish the results of all of them.



## UK to Force Drugmakers to Share Info

Britain plans to force pharmaceutical companies to share more information with regulators about clinical trials after an investigation recently concluded that GlaxoSmithKline PLC deliberately withheld information about an antidepressant.

The four-year probe by the Medicines and Healthcare products Regulatory Agency, completed earlier this month, said the British company should have revealed more quickly that Seroxat sometimes increased the suicide risk in teenagers - by more than six times.

But without stronger legislation in place, the MHRA admitted there is no chance of prosecuting the company for what the agency perceives as an ethical lapse. "I remain concerned that GSK could and should have reported this information earlier than they did," MHRA chief executive Kent Woods said in a statement.

GlaxoSmithKline rejected the suggestion that it withheld information. "We firmly believe we acted properly and responsibly," said Dr. Alastair Benbow, the company's European medical director. British legislation only obliges companies to report side effects in patients for which drugs are officially recommended.

Because Seroxat was only recommended for adults, GlaxoSmithKline was not required to report on any dangerous side effects it found in adolescents.

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## Anti-depressants' 'little effect'

*New generation anti-depressants have little clinical benefit for most patients, research suggests.*

A University of Hull team concluded the drugs actively help only a small group of the most severely depressed. They reviewed published clinical trial data, and **unpublished** data secured under Freedom of Information legislation.

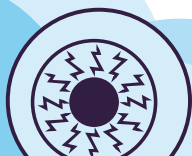
The researchers found that the drugs did have a positive impact on people with mild depression - but the effect was no bigger than that achieved by giving patients a sugar-coated "dummy" pill.

Lead researcher Professor Irving Kirsch said: "The difference in improvement between patients taking placebos and patients taking anti-depressants is not very great. "This means that depressed people can improve without chemical treatments." Professor Kirsch said the findings called into question the current system of reporting drug trials.

[bbc.co.uk/news](http://bbc.co.uk/news) 26th Feb 2008

**Your task.** Get into groups of three.

1. Can you think of three reasons why the scientists hadn't published all of their research on anti-depressants?
2. Do you think drugs are the best way to treat depression? Suggest two alternatives.
3. Can you suggest two other diseases which non-drug treatments could help with? What treatments?
4. Think about if there could be any publication bias in the areas the IAS scientists work on. How could you check?



**Peer review** is part of how science is **quality controlled**.

**Before** a scientist can publish their work other experts assess the quality of work, research or ideas. All the experts will be from the same field of science. These experts should have **no links** to the person who completed the study or anyone else involved in it. Otherwise they might be able to 'do them a favour' and say their work is OK when really it's not.

This process makes sure that what gets published is as **accurate** as it can be. But it can't do much about things that **aren't** published...

### A drug's journey...

All drugs go through a tough **trials process** that will take over 10 years and pass through all of the following stages. Only if a drug performs well in one phase will it go to the next one.

The process will start when a scientist or a team of scientists find a **compound** that looks like it could be useful in treating a disease and will carry out tests. If they are sure that it could be useful as a drug they will start the **preclinical trials**, although at this stage the chances the compound will make it onto the market as a drug are very slim!

**Preclinical trials** will test how the drug will break down in the body, the effect it will have and how the body will process it. The drug will be tested in test tubes and in animals. Once scientists are sure it is safe and will have the desired effect on the body they will start the trial itself.

**Clinical trials** test the drug on humans to check whether it is safe and whether it works. These are in three phases with more people in each trial. If a drug passes this point it will get a licence but will continue being tested to make sure it safe. This is called phase IV. Only a few percent of the 'useful compounds' identified at the start of the process will make it this far!!

### Understanding publication bias

When you were younger, did you ever show your parents your school coursework when it had been marked?  
Did you show them all of your coursework, or only some?  
If you only showed them some, was it at random, or were you more likely to show them things where you'd got a good mark?  
Did they get a better idea of how you were doing at school from your exam results, or from the individual bits of coursework you showed them?

'**Publication bias**' is a term to describe the fact that **positive, significant or interesting** results are more likely to be published than negative, or neutral ones.

This can be **unintentional** – just because people are more likely to get round to writing up positive or interesting results. Scientists are people too and can take longer to get round to writing up boring or inconclusive results.

This is sometimes called the 'file drawer problem'.

Or it can be **intentional** – because organizations may not like negative results or want to publicise positive results more.

For agencies like the MHRA to make decisions about drugs, or even for the public to make a decision about something, they need all relevant data. Otherwise it's like trying to make your mind up about something when you only have half the story.

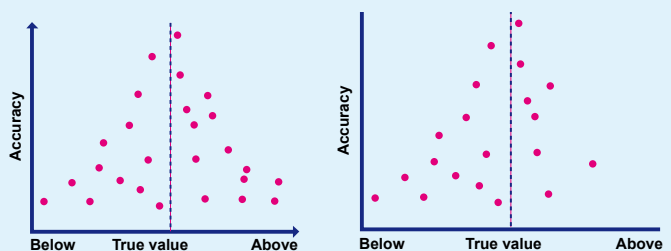


### How can you spot publication bias?

Big, extensive studies should give you more accurate results than smaller ones. You can plot all the studies done on something on a graph, with the accuracy of the study plotted against the value found.

The graph should look like an upside-down funnel. The biggest studies should all cluster round the true value. The smaller (and therefore less accurate) studies should be more spread out - above and below the true value.

If part of the funnel is missing – you've got more studies on one side than the other – then that suggests that there has been some publication bias and not all the studies have been published.



Which funnel plot shows publication bias?

